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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,639	10/23/2003	Juan Lopez de Silanes	2099.0010001/JAG/LAV	9165

26111 7590 07/03/2007

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EXAMINER	
KIM, YUNSOO	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
07/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/690,639	**Applicant(s)** DE SILANES ET AL.
	Examiner Yunsoo Kim	**Art Unit** 1644

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 June 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *15 June 2007*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *30,31,36,44,45,67 and 74-78*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☒ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 5. Applicant's reply has overcome the following rejection(s): 35 USC 112 1st enablement (sec 3-4 of the office action mailed 12/15/06).

Continuation of 11. does NOT place the application in condition for allowance because:

Claims 30, 31, 36, 44, 45, 67 and 74-78 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S.Pat. No. 5,443,976, of record, in view of U.S. Pat. No. 4,849,352 (IDS reference, of record) as evidenced by Harlow and Lane (Antibodies, 1988, Cold Spring Harbor Lab., p.298-299, of record) and Campbell (Monoclonal and Immunosensor Technology, 1991, Elsevier, vol. 23, p. 288-291, of record) for the reasons set forth in the office action mailed 12/15/06.

The '976 patent teaches IgY polyclonal antibody to a scorpion venom, Centruroids noxius (col. 11, lines 43, Example 52, in particular).

The '976 patent does not teach F(ab')2 fragments.

However, the '352 patent teaches a pharmaceutical composition comprising a polyclonal F(ab')2 binds to any antigen, pepsin digested followed by ammonium sulfate precipitation (col 3, lines 22-41, col. 2, lines 51-65, in particular).

The '352 patent further teaches that the antibody fragments are quickly distributed in the body, filtered and excreted by the kidney. Toxin neutralization by antibody fragments and volume circulating are greater than IgG (col. 1-2 overlapping paragraph, in particular).

The limitation " pharmaceutical" is met as the purified antibody after dialyzed against distilled water (e.g. pharmaceutically acceptable carrier, col. 8, lines 8-50, in particular) and 100ul of antibody injected to Swiss Webster mice (col. 11, lines 1-10, in particular). In addition, " substantially free of albumin, pyrogens and viral particles" is inherent property of any antibody purified by pepsin digestion and ammonium sulfate precipitation.

It is well known in the art as evidenced in Harlow and Lane (p. 299, in particular), repeating the precipitation process as necessary is within the optimization of procedures. Furthermore, the range of the first ammonium sulfate precipitation at about 16-22% and the second precipitation at about 32-38% is taught in Harlow and Lane as further evidenced by Campbell.

Campbell defines 100% saturated ammonium sulfate having 770g/l. Harlow and Lane suggest addition of 0.5 volume and to 50% saturation of saturated ammonium sulfate (step. 3, p. 29, in particualr) to antibody solution which results 1.5 total volume. The final concentration of ammonium sulfate is ~250g/l, which is equivalent to 25% by weight.

The concentration range of the second ammonium sulfate precipitation is met by addition of ammonium sulfate to 50% saturation (step 4), having 770g/l, 50% saturation is equivalent to 385g/l, or 38.5% by weight.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to pepsin digest and purify with ammonium sulfate as taught by the '352 patent with the polyclonal and polyvalent antibody taught by the '976 patent.

The one of ordinary skill in the art would have been motivated to do so because the digestion with pepsin and purification with ammonium sulfate as taught by the '352 patent with the polyclonal and polyvalent combine antibody to scorpion venom Centruroids noxius taught by the '976 patent produces more readily utilizable antibody to scorpion venom. The '352 patent teaches intact IgG is too large to excreted by kidney functions and antibody fragments excrete many kinds of neurotoxins that are not accessible to IgG (col. 2, lines 22-50, in particular).

From the combined teachings of references, one of ordinary skill in art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary skill in the art at the time the invention was made, as evidenced by references, especially in the absence of evidence to the contrary.

Applicants' arguments filed on 6/15/07 have been fully considered but they were not found persuasive.

Applicants traversed the rejection based on the examiner's failure to satisfy the reasponable expectation of success upon combination of teachings of the references because of examiner's statements regarding Burton et al (of record) and Valandschool et al (of record) that "not all animal venoms are equally feasible in prophylactic measures" and that "not all antibodies are neutralizing". Therefore, it is not obvious to combine reference teachings.

The above mentioned statements are provided in the 35 U.S.C. 112 1st , enablement rejection to show why the instant specification lacks the specific guidance to practice the claimed invention.

However, contrary to Applicants' arguements, the referenced '976 patent particularly teaches the antibodies are neutralizing venom (col. 9-10, overlapping paragraph col. 62, Table 10, in particualar) and the particualr antibodies are used in vivo. Given that the '976 patent particularly teaches the neutralizing polyclonal antibody to scorpion venom, Centuroid noxius, the claimed limitations regarding "neutralizing a purified antigenic molecule" and "pharmaceutical" are satisfied.

In light of discussion above, the combination of teachings remains obvious.

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June 28, 2007

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